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"A PROCESS RELATING TO THE PRODUCTION OF 3- CYANOPYRIDINE FROM 3- PICOLINE"

COUNCIL OF SCIENTIFIC AND INDUSTRIAL RESEARCH, RAFI MARG, NEW DELHI-1, INDIA, AN INDIAN REGISTERED BODY INCORPORATED UNDER THE REGISTRATION OF SOCIETIES ACT, (ACT XXI OF 1860).

The following specification particularly describes and ascertains the nature of this invention and the manner in which it is to be performed :—

This is an invention by SISIR KUMAR ROY, KRISHNADEO PRASAD SHARMA, SAMIRAN BASU, NADIMINTI VENKATA RAMANA APPA-RAO, HEJAMADI SHREEPATHI RAO and ADI NATH LAHIRI, all of the Central Fuel Research Institute, Jealgora, P. O. F. R. I., Dist. Dhanbad, Bihar, and all Indian Citizens.

This invention relates to a process relating to the production of 3-cyanopyridine from 3-picoline

INTRODUCTION AND INVENTION MERITS:

Nicotinic acid and its amide (pp Vitamin) are widely used as additives in food and fooder production to improve human and animal nutrition for faster growth and better health. This vitamin not only aids in preventing and curing pellagra, but plays a key role in protein and carbohydrate metabolism. In the body nicotinic acid is converted into its amide which is an essential constituent of Co- enzymes I and II involved in the oxidation of carbohydrates.

The feed grade nicotinic acid (purity about 98%) used in zootechny, represents about 60—65% of the total consumption of nicotinic acid and amide, whereas the best products (USP nicotinic acid and amide purity about 99.5%) are used for pharmaceuticals.

Generally feed grade nicotinic acid is sold in the market as 50—50 mixtures with different additives (e.g. Soyabean meal). In the nutrition of calves for instance 0.2—0.4 lbs of these mixtures are added to a ton of fodder.

Nicotinic acid is also used in may pharmaceutical preparations, the most important of which are, nicotinic acid diethylamine, a cardiac stimulant, 1-nicotinamide 1-2 diphenylethane, an anti-spasmodic, nicotinates of methyl, ethyl, benzyl, guiacyl and phenyl-dimethyl- pyrazol- one for use as anti-rheumatics and hexanicotinate of inositol for fortifying the action of inositol.

It has hitherto been the practice to prepare these drugs from 3-picoline via nicotinic acid obtained by oxidation of the former with nitric acid or potassium permanganate. However, this procedure suffers from the disadvantage that the overall yields are not sufficiently high. Further, the oxidation processes for nicotinic acid from 3-picoline employing nitric acid or permanganate involve batch treatment and are not amenable to operation on a continuous basis with the associated advantages thereof.

Although attempts have been made to produce nicotinic acid by catalytic vapour phase oxidation of 3-picoline with either air or oxygen, the yields reported so far have been quite unsatisfactory. The economic unsuitability of any process where the yields are not high becomes apparent when the high price and scarce nature of the feed-stock (3-picoline) is taken into consideration.

In the absence of a suitable procedure for the direct vapour phase oxidation of 3-picoline to the corresponding acid, the profitability of converting 3-picoline via the cyanoderivative into the correspondng acid or ester becomes apparent.

While procedures are available for the production of 3-cyanopyridine from pyridine, via the bromoderivative or via pyridine sulphonic acid, these are tedious, hazardous and do not give high yields. The use of 3 picoline in place of pyridine for the production of 3-cyanopyridine therefore suggests itself as an alternative, if a convenient synthetic route could be developed, and this has been accomplished in this invention.

The novelty of this invention lies in the vapour phase transformation of 3-picoline into 3-cyanopyridine, in a single step, though the reaction between the base, ammonia and air to give a high yield of pure product thus eliminating the need for expensive oxidising agents and enabling the operation of the process on a continuous basis.

According to the present invention, there is provided a process for the production of 3-cyanopyridine by reacting 3-picoline, air and ammonia commonly known as ammoxidation, followed by recovery of both 3-cyanopyridine and 3-picoline characterised in that the ammoxidation is carried out in the vapour phase at 390°C in the presence of vanadium pentoxide-molybdenum trioxide -phosphorous pentoxide—alumina as catalyst.

Un-reacted 3-picolene in recovered and recycled.

Vanadium pentoxide-molybdenumtrioxide-phosphorus pentoxide-alumina in the ratio of (25 : 4 : 0.2 : 70.8) may be used as the catalyst.

3-Cyanopyridine is trapped by cooling at 10°C and the unreacted 3-picoline is recovered by either refrigeration or through absorption in sulphuric acid, the 3-picoline being released for recycling from the condensate by distillation and from the picoline sulphuric acid salt by neutralisation with alkali and extraction with ether, followed by distillation.

The yield of 3-cyanopyridine is about 83 gm. per pass and that with recycling of the unreacted 3-picoline is more than 90 gm., for every 100 gm. of 3-picoline charged.

The formation of nicotinic acid and pyridine is totally eliminated.

The catalyst is reactivated over a running stream of air at 450°C.

This invention where air and ammonia are used for the ammoxidation reaction results in 3-cyanopyridine, which when worked up appropriately, satisfies the required specifications for utilisation in the manufacture of both ethical and proprietory drugs and food additives.

Application of the invention should make possible the transformation of 3-picoline into 3-cyanopyridine and should result in nicotinic acid or its amide, the hydrolysis product of 3-cyanopyridine, becoming readily available for the production of pharmacological intermediates, vitamins and drugs.

The invention claims to make possible the direct conversion of 3-picoline to 3-cyanopyridine that is in

immediate demand for the production of drugs and pharmaceuticals like nicotinic acid, nicotinamide and coramine; thus providing a convenient route for the production of this key organic intermediate for utilisation in the drugs and pharmaceutical industries.

The following is a description of the process, as it has been operated on the laboratory scale.

(1) The transformation of 3-picoline to 3-cyanopyridine is carried out at a reaction temperature of 390°C in a stainless steel reactor mounted in a vertical tubular furnace and packed in three sections. First, a one-half length of the reactor tube is packed with unglazed porcelain beads, this being followed by the catalyst mass (—6, +14 mesh, B.S.) comprising one-third of the reactor tube length, after which is placed another layer of insulating beads corresponding in length to one-quarter of the catalyst bed depth. The reactor tube, the inert suppor and the catalyst mass are heated and maintained at the requisite reaction temperature for two hours. The feeder line is provided with a picoline "well" whose temperature is raised and maintained at the desired value using an electrically heated blanket. Air and ammonia are mixed before being bubbled through the picoline well. The stream of air and ammonia entrains with it the requisite quantity of picoline vapour, the desired proportion being adjusted by controlling the temperature of the picoline "well".

(2) Catalyst :

Of the various catalysts that were tried, vanadium pentoxide—molybdenum trioxide—phosphorus pentoxide on alumina prepared as described herein gievs the best results.

To a saturated solution of aluminium nitrate, a 50% solution of ammonium hydroxide was added till the pH reached a value between 7 and 8. The resulting gel of aluminium hydroxide was allowed to settle, washed by decantation repeatedly till free from the nitrate ion and filtered through a buchner funnel. The solid mass so obtained was first dried in an air oven for about 6 to 8 hours at approximately 140°C, subsequently heated in a tubular furnace at 450°C under a running stream of air, following which it was reduced to proper size and heated in a muffle furnace at 450°C for 6 hours.

The required vanadyl sulphate was prepared by bubbling sulphur dioxide gas (generated by dropwise addition of 50% hydrochloric acid over sodium metabisulphite) through a suspension of vanadium pentoxide in 16% sulphuric acid.

In quantities corresponding to a catalyst composition

Vanadium pedtoxide	: Molybdenum trioxide	: phosphoros pentoxide	: Alumina
25	4	0.2	70.8

the alumina is impregnated with the requisite quantity of vanadyl sulphate, molybdenum trioxide and phosphoric acid. The resulting mass was first dried on a water bath, following by second stage drying in an air oven for six hours at 130—140°C. The dried mass was next baked at 450°C in a tubular furnace under a running stream of air for six hours, reduced to proper size (—6 to +14 B.S.) and again heated in a muffle furnace for 5 hours at 450°C.

(3) The reaction products are collected in three sets of condersers, the first cooled with air, the second with circulating water at 10°C and the third under crushed ice and salt mixture. The major part of 3-cyano-pyridine is trapped in the air condensers, the ice-cooled trap holding the residual 3-cyanopyridine along with a trace of unreacted 3-picoline The bulk of the unreacted picoline is still contained in the outgoing stream of air and ammonia, and is isolated either by refrigeration effecting near quantitative recovery or by absorption in 50% sulphuric acid. The production corresponds to 83 gm. of 3-cyanopyridine for every 100 gm. of 3-picoline charged.

The process is schematically illustrated in the accompanying Flow Diagram.

WE CLAIM :

1. A process for the production of 3-cyanopyridine by reaching 3-picoline, air and ammonia commonly known as ammoxidation, followed by recovery of both 3-cyanopyridine and 3-picoline characterised in that the ammoxidation is carried out in the vapour phase at 390°C in the presence of vanadium pentoxide-molybdenum trioxide phosphorus pentoxide -alumina as catalyst.

2. A process as claimed in claim (1) wherein unreacted 3-picolene in recovered and recycled.

3. A process as claimed in claim 1 or 2 wherein vanadium pentoxide-molybdenumtrioxide-phosphorus pentoxide-alumina in the ratio of (25 : 4 : 0.2 : 70.8) is used as the catalyst.

4. A process as claimed in any of the preceding claims wherein 3-cyanopyridine is trapped by cooling at 10°C and the unreacted 3-picolene is recovered by either refrigeration or through absorption in sulphuric acid, the 3-picoline being released for recycling from the condensate by distillation and from the picoline-sulphuric acid salt by neutralisation with alkali and extraction with ether, followed by distillation.

5. A process for the production of 3-cyanopyridine substantially as hereinbefore described.

Dated this 13th day of September, 1972.

(Sd.)
PATENTS OFFICER,
Council of Scientific & Industrial Research.

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NO. OF SHEET 1
SHEET NO. 1

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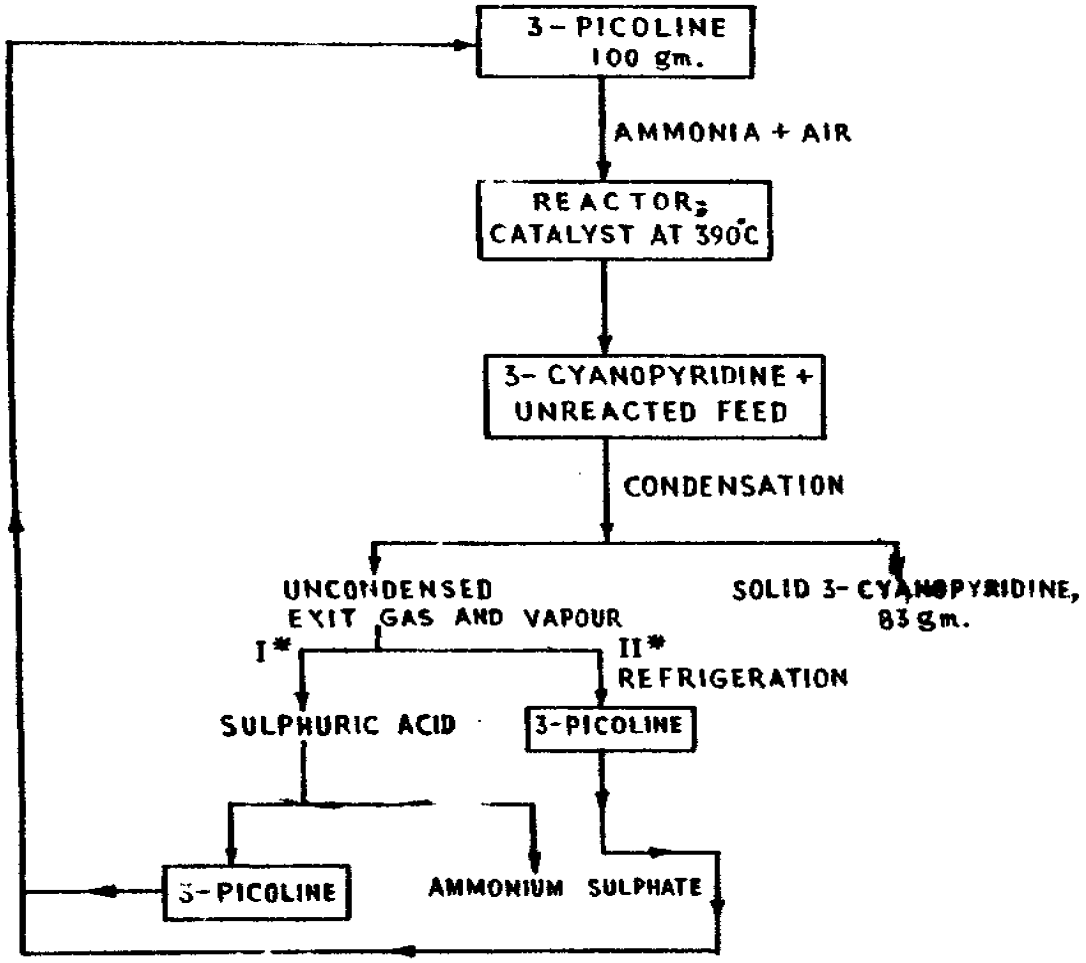
FLOW DIAGRAM



*RECOVERY AND RECYCLING OF 3-PICOLINE IS EFFECTED EITHER VIA I OR ALTERNATELY VIA II.

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